REMARKS

Applicants acknowledge the current status of the claims, as reported in Office Action dated 11 May 2007: Claims 4-8, 11-30, 32-88 and 96-104 are pending; claims 5-8, 11, and 32-88 are withdrawn from consideration; claims 4, 12-30 are allowable; and claims 96-104 stand rejected.

Applicants thank the Examiner for the courtesy of Examiner's interview, conducted on 09 October 2007, to discuss the bases of the outstanding rejections to Applicants' application. This interview forms the basis for the present remarks.

Claims 96 and 97 have been amended to recite Applicants' dual specific antibody is not a fully mouse antibody. Support for these amendments can be found throughout the specification as filed, and particularly at pages 29-30. No new matter is added.

Reconsideration and allowance of the pending claims in light of the foregoing amendments, and following remarks, are respectfully requested.

Rejections under 35 USC §103(a)

In the Office Action, starting at page 2, paragraph 4, rejection of claims 96-104 under 35 USC §103(a) are maintained as being unpatentable over Luger et. al., Immunobiology, 1986, vol. 172, pp. 346-356 in view of Schmidt et. al., (EP0218531) and Berg (US Patent 5622701). The Examiner continues to assert that "it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made a dual specificity antibody with enhanced sensitivity against both IL-lα and IL-1β." Specifically, the Examiner relies on the disclosure of Schmidt et al. to conclude "The ten amino acid sequence peptide of Schmidt et al., combined with the sequence overlap with the four amino acids that are potential antigenic epitopes of both IL-lα and IL-l β is sufficient to permit antibodies raised against the peptide of Schmidt et al., to be used to bind both IL- lα and IL-1β." Applicants respectfully disagree.

For purposes of advancing examination of the present application to allowance only, Applicants have amended claims 96 and 97 to recite that Applicant's dual-specificity antibody, or antigen-binding portion thereof, that specifically binds interleukin-1α and interleukin-1β, and wherein said dual-specificity antibody, or antigen-binding portion is capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ (SEQ ID NO: 3) is not a fully mouse antibody. Support for dual-specificity antibodies other than mouse antibodies can be found throughout the specification as filed and particularly at pages 29-30. Furthermore, negative limitations, or claim exclusion by proviso, is proper patent practice, provided such limitations are sufficiently definite (see MPEP 2173.05(i)). Applicants

assert the recited antibodies are sufficiently definite and the boundaries of the patent protection sought are sufficiently clear to render Applicant's negative limitation proper. (See also *In re Wakefield*, 422 F.2d 897, 899, 904, 164 USPQ 636, 638, 641 (CCPA 1970). *In re Barr*, 444 F.2d 588, 170 USPQ 330 (CCPA 1971). *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977).). Applicants reserve the right to prosecute excluded subject matter in a later-filed continuation application, which properly claims the benefit of this application.

The Examiner asserts that the rejection of claims 96-104 under 35 USC §103(a) meets all of the prima facie requirements under Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) and KSR INTERNATIONAL CO., v. TELEFLEX INC. ET AL., 127 S. Ct. 1727 (2007). Applicants respectfully disagree. While the court in KSR v. Teleflex rejected the rigid construction of the Teaching, Suggestion and Motivation (TSM) test applied when all the elements are independently known in the prior art, the court did not reject the "all-elements" requirement for obviousness. It is well settled that all elements of a claim must be present to establish a proper *prima facie* case of obviousness. There is no, "motivation", "modification", or "reasonable expectation" component to the all elements criterion for establishing *prima facie* obviousness; ALL claim limitations must be taught or suggested in the cited art (MPEP 2143.03).

As amended, claim 96 is directed to a dual-specificity antibody, or antigen binding portion thereof, that;

i) specifically binds interleukin-1α and interleukin-1β, wherein said dual-specificity antibody, or antigen-binding portion

ii) is capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ (SEQ ID NO: 3)

iii) is not a fully mouse antibody.

Claims 97-104 recite further specific embodiments of Applicants' invention wherein Applicants' dual-specificity antibody is; a fully human antibody (claim 98), a chimeric antibody (claim 99), a CDR grafted antibody (claim 101) or a humanized antibody (claim 104).

Luger et al. disclose a mouse monoclonal antibody that cross-reacts with IL-1α and IL-1β. Luger et al. do not teach an antibody, or antigen binding portion thereof, capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ wherein said antibody is not a fully mouse antibody.

Schmidt et al. disclose peptides derived from IL-1β and antibodies to those peptides. Specifically, Schmidt et al. disclose an antibody to the amino acid sequence THR LYS GLY GLY GLN

ASP ILE THR ASP PHE THR (i.e., TKGGQDITDFT) (Claim 1, page 11, line 2). Schmidt et al. do not teach or suggest an antibody, or antigen binding portion thereof, capable of binding IL-1α and IL-1β, and capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ.

Berg discloses monoclonal antibodies capable of binding P-Selectin and E-Selectin. Berg does not teach or suggests an antibody, or antigen binding portion thereof, capable of binding IL-1α and IL-1β. Berg does not teach or suggests an antibody capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ.

Applicants assert that none of the cited art, singularly, or in combination, teach or suggest all claim limitations. For example, Luger et al., Schmidt et al., and Berg all fail to teach or to suggest the explicitly recited feature of Applicants' claimed antibody namely it binds interleukin-1α and interleukin-1β, it is capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ(SEQ ID NO: 3), and it is not a fully mouse antibody.

The Examiner relies on the disclosure of Schmidt et al., citing the feature that one of the disclosed peptides of Schmidt et al. (i.e, TKGGQDITDFT) shares a ten amino acid sequence in common with the sequence recited in Applicant's claimed invention (i.e, TKGGQDITDFQILENQ).

As stated in the paper filed on 15 February 2007, the disclosed peptide of Schmidt et al. is not the peptide recited in Applicants' claimed invention. Not only is the antigenic sequence of Applicants' invention significantly longer than that disclosed by Schmidt et al., the recited amino acid sequences of the two polypeptides are, in fact, different in their amino acid sequence. Amino acid sequence defines the primary structure of a polypeptide. Polypeptides of different amino acid sequence are, in fact, structurally different. Schmidt et al. fails to provide the antigenic binding feature of Applicants claimed antibody in satisfaction of the all elements requirement to establish a *prima facie* case of obviousness.

The Examiner asserts that "The ten amino acid sequence peptide of Schmidt et al., combined with the sequence overlap with the four amino acids that are potential antigenic epitopes of both IL-lα and IL-l β is sufficient to permit antibodies raised against the peptide of Schmidt et al., to be used to bind both IL- lα and IL-1β." Applicants respectfully disagree.

As an initial matter, the cited Schmidt et al. peptide sequence is not a "ten amino acid sequence peptide" as asserted by the Examiner. The Schmidt et al. peptide is an eleven amino acid peptide, whose primary sequence structure is different from that of Applicants' antigenic peptide. The Examiner has improperly characterized the disclosed Schmidt et al. peptide sequence in an effort to "deconstruct" the Schmidt et al. peptide (modification by amino acid residue truncation), and then to "reconstruct" a peptide (modification by amino acid residue additions) into Applicant's recited antigenic peptide.

Notwithstanding the above, and by the Examiner's own admission, the deconstructed Schmidt et al. peptide is "**combined** with the sequence overlap with the four amino acids that are **potential** antigenic epitopes' of both IL-lα and IL-l β" (emphasis added). Applicants' assert that such modification and "combination" with a four amino acid sequence, not taught or suggested in the cited art is improper. In addition, the improperly reconstructed peptide, having a "potential" to be antigenic, is nothing more than speculation (absent Applicants' specification) on the part of the Examiner, and as such is improper.

The Examiner cites Harlow et al., Eds. Antibodies, A Laboratory Manual, 1988 Cold Spring Harbor Lab, and asserts that Harlow et al., "teach that small synthetic peptides with six amino acid residues in length will consistently elicit antibodies that bind to the original peptide." The Examiner further asserts that Harlow et al., teach antibodies to even smaller peptides, but that peptides of approximately 10 residues should be used to generate antibodies. Based on this the Examiner concludes that the four amino acids (ITDF) contained in the cited Schmidt et al. peptide, also found in Applicants' peptide would be sufficient to raise antibodies capable of binding IL-lα and IL-l β. Applicants respectfully draw the Examiner's attention to the fact that Schmidt et al. teach antibodies that are monospecific for human IL-1 β, and a method of making such monospecific antibodies to human IL-1 β using peptides derived from human IL-1 β. Thus, the Examiner's conclusion that the four amino acids (ITDF) contained in the cited Schmidt et al. peptide, also found in Applicants' peptide would be sufficient to raise antibodies capable of binding IL-lα and IL-l β is mere speculation.

Examiner asserts that the rejection of claims 96-104 under 35 USC §103(a) is amenable to evidence. The Examiner states that 'because the Patent Office does not have the facilities to determine whether the antibodies of Luger et al., made against the peptide of Schmidt et al., and humanized by the modifications of Berg overlap with the instantly claimed dual-specificity antibodies, the burden is on the application to show a novel and unobvious difference between the claimed antibodies and that of the prior art." In fact, in the case cited by the Examiner, Ex Parte Gray, 10 USPQ 2d 1922, 1924-25 (PTO Bd. Pat. App &Int.), the court cited In re Best, 195 USPQ 433-434 where the court held that "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product." Applicants respectfully submit that Applicants' claimed antibody is neither identical nor substantially identical to the prior art antibodies. As stated supra, Luger et al. disclose a mouse monoclonal antibody that cross-reacts with IL-1α and IL-1β. Luger et al. do not teach an antibody, or antigen binding portion thereof, capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ wherein said antibody is not a fully mouse antibody. Schmidt et al. disclose peptides derived from IL-1β and

antibodies to those peptides. Specifically, Schmidt et al. disclose an antibody to the amino acid sequence THR LYS GLY GLY GLN ASP ILE THR ASP PHE THR (i.e., TKGGQDITDFT) (Claim 1, page 11, line 2). Schmidt et al. do not teach or suggest an antibody, or antigen binding portion thereof, capable of binding IL-1α and IL-1β, and capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ. Applicants' claimed antibody is not produced by identical or substantially identical processes used in the cited art. Applicants used an artificially created antigen, TKGGQDITDFQILENQ (SEQ ID NO: 3), as disclosed in the Example section of the specification, to generate their dual-specificity antibodies. Luger et al. generated their antibody using IL-1 isolated from human peripheral blood adherent cells. Schmidt et al., generated their monospecific antibodies to human IL-1 β using peptides derived from human IL-1 β. In view of the foregoing, the Examiner's assertion that Applicants must provide evidence that the antibodies of Luger et al., made against the peptide of Schmidt et al., and humanized by the modifications of Berg do not overlap with the instantly claimed dual-specificity antibodies is improper and based on nothing more than speculation (absent Applicants' specification).

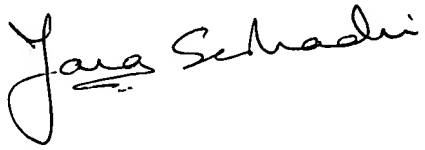
Because the cited prior art fails to teach or to suggest Applicants' claimed antibody "capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ(SEQ ID NO: 3), as an element of Applicants' claimed invention, the present rejection fails to satisfy the all elements criterion that a *prima facie* case of obviousness must satisfy.

Because the cited art fails to satisfy the criteria necessary to establish or to sustain rejection of claims 96-104 as obvious under 35 USC §103(a), and in view of the foregoing remarks, Applicants respectfully request withdrawal of the rejection of claims 96-104 under 35 USC §103(a).

Conclusion

In view of the foregoing amendment and remarks, Applicants believe that all objections and rejections set forth in the Office Action of 11 May 2007 have been obviated or overcome, and consequently the application is in condition for allowance. Reconsideration, withdrawal, and removal of the rejections, and allowance of the pending amended claims are, therefore, respectfully requested.

Respectfully submitted,



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